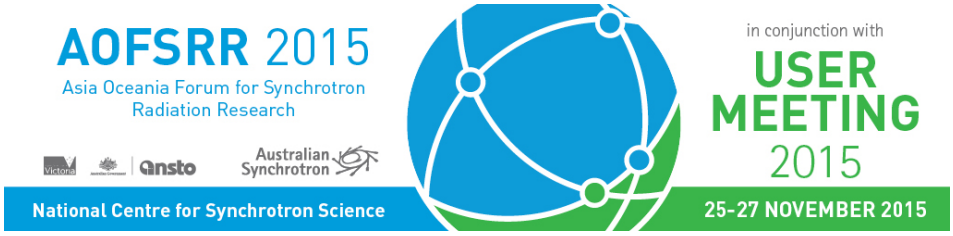

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Structura Insights into the pro-apoptotic protein Bax

Thursday, 26 November 2015 13:30 (45)

Programmed cell death, AKA apoptosis, is a biological mechanism by which dangerous cells, such as cancer cells, are killed. Commitment to this process is governed by the Bcl-2 family of proteins, which respond to cellular stresses. The proteins within this family share 1 to 4 Bcl-2 Homology domains (BH1 to BH4) and can be divided in three sub-categories according to their function. One subgroup, the BH3-only proteins, is up-regulated upon cellular stresses and initiate apoptosis through interactions with other Bcl-2 family members. Another subgroup, the pro-apoptotic Bax or Bak proteins, are the effectors of apoptosis: upon activation these proteins oligomerize at the mitochondrial outer membrane and provoke its permeabilization. The resulting release of cytochrome c and other pro-apoptotic proteins leads to cell death.

The BH3-only proteins Bim and Bid can directly activate Bax or Bak. Recently the structure of the BidBH3 in complex with the hydrophobic groove of Bax enlightened how BH3-only proteins activate the Bax protein. [Czabotar, Westphal et al., Cell, 2013, 152, 519-531.] We have now crystallized new forms of Bax:
1- Novel structures of full length monomeric Bax and P168G mutant of Bax show the hydrophobic groove of Bax occupied by the trans-membrane helix 9 of Bax.
2- BimBH3:Bax complexes structures help us to understand the specifics of the BimBH3 peptide binding to the hydrophobic groove of Bax.

These new structures reveal further insights into key interactions that initiate Bax activation.

Keywords

Apoptosis, Bax, Bim

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